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Does composite bone resection for soft-tissue sarcoma with cortical contact result in better local control and survival compared to sub-periosteal dissection?

A comparative retrospective cohort study

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Aims
Osseous invasion exhibited in soft-tissue sarcoma (STS) is recognized as a prognostic risk factor. Achieving a wide margin is the default surgical approach for local control. However, for STSs where the tumour is in contact with the adjacent cortex but without clear evidence of osseous invasion, such as medullary invasion, the question of whether bone resection can provide better local control or survival than more conservative sub-periosteal excision remains controversial. The aim of this study was to assess whether bone resection for thigh STS with cortical contact of the adjacent bone results in better local control and survival compared to sub-periosteal dissection, and to investigate the prognostic factors for clinical outcomes in STS.

Methods
A retrospective cohort study was conducted on 142 patients with thigh STS exhibiting cortical contact but without medullary invasion, from May 2000 to May 2020. Patients underwent either composite bone resection or sub-periosteal excision. Demographics, clinical outcomes, and functional outcomes were compared between the two groups. Additionally, Cox regression analysis was used to analyze risk factors for local recurrence.

Results
The five-year overall survival, local recurrence-free survival, and metastasis-free survival among patients with bone resection was 74.0%, 65.9%, and 74.1%, respectively, compared to 72.9%, 68.3%, and 72.0%, respectively, among patients with sub-periosteal excision. The cumulative incidence of recurrence was 33.1% for patients who underwent bone and 36.4% for those with sub-periosteal excision ($p = 0.681$). In multivariate analysis, STS with high Fédération Nationale des Centres de Lutte Contre Le Cancer (FNCLCC) grade, invasion involving posterior intermuscular septum, medial intermuscular septum, and adductor brevis were found to be associated with poorer prognosis. The mean Musculoskeletal Tumor Society (MSTS) score in the bone resection group was 24.7, significantly lower than the 28.3 in the sub-periosteal group ($p < 0.001$).

Conclusion
Routine bone resection failed to improve local control or survival in STS patients with cortical bone contact, but resulted in significantly impaired postoperative function. A more conservative sub-periosteal excision approach may be preferable for these cases.

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Take home message

- For soft-tissue sarcoma with cortical bone contact, but no medullary invasion, composite bone resection does not improve local control or survival compared to sub-periosteal excision. On the contrary, it significantly impaired postoperative function.
- Bone resection merits meticulsouly consideration in this particular group of patients.

Introduction

Soft-tissue sarcoma (STS), a rare type of malignancy that arises from mesenchymal tissues, constitutes approximately less than 1% of all malignant adult solid tumours.[1] Prognostic factors for oncological outcomes in limb STS have been thoroughly investigated in various studies. Multiple factors, particularly histological grade, clinical stage, and resection margin, are widely acknowledged to be associated with the prognosis of STS.[2–5]

Osseous invasion in STS has been widely acknowledged as a poor prognostic indicator, often necessitating aggressive surgical approaches such as composite bone resection to ensure an adequate margin for local control.[6] However, cortical contact occurs when the tumour is in direct contact with the adjacent bone but does not breach the cortex to involve the medullary canal. For these equivocal cases, osseous invasion can only be confirmed via postoperative pathological assessment. Surgeons are unable to determine the existence of genuine osseous invasion based on preoperative imaging.[6,7] Therefore, whether to conduct composite bone resection or more conservative sub-periosteal excision remains controversial.

The uncertainty surrounding the appropriate surgical approach for tumours with cortical contact lies in the balance between oncological safety and functional preservation. Bone resection may add morbidity without clear evidence of improved prognosis, while sub-periosteal dissection offers a more conservative approach that preserves bone structure. Whereas periosteum has been considered as a barrier against sarcoma invasion,[8] concern persists among surgeons regarding recurrence due to microscopic tumour residual on the sub-periosteal resection margin of the cortex, as the likelihood of obtaining a wide margin is not feasible without bone excision.

Therefore, the purpose of the current study was to assess whether bone resection for thigh STS with cortical contact of the adjacent bone results in better local control and survival compared to sub-periosteal dissection. Additionally, we aimed to investigate the prognostic factors for clinical outcomes in this group of STSs.

Methods

Patient characteristics

Table I shows the demographic comparison of 142 patients, with 37 (23.3%) undergoing bone resection and 105 (76.6%) undergoing sub-periosteal excision. Patients in the bone resection group had higher rates of FNCLCC grade III (64.9% vs 52.4%), tumours > 10 cm (89.2% vs 81.9%), and > 50% circumferential bone involvement (27% vs 17.1%). Nevertheless, no significant differences were observed between the groups regarding the aforementioned characteristics and other patients' characteristics (e.g. age, sex, and chemotherapy/radiotherapy use). Full-course radiotherapy was completed more commonly in patients who underwent sub-periosteal excision (34 out of 105; 32.4%) than those with bone resection (six out of 37; 16.2%). The distribution of histological subtypes varied between groups, with undifferentiated pleomorphic sarcoma (UPS), liposarcoma, chondrosarcoma, and Ewing's sarcoma predominating in the bone resection group, while no chondrosarcoma or Ewing's sarcoma was seen in the sub-periosteal group.

Inclusion/exclusion criteria

With approval of the institutional ethics committee of the Second Affiliated Hospital of Zhejiang University School of Medicine, from May 2000 to May 2020, a total of 1,020 patients diagnosed with primary thigh STS, who received primary surgery at our centre, were selected for initial screening. Only patients who underwent limb salvage surgery were included in this study, and they were divided into two groups: 1) patients who underwent bone resection following either biological or endoprosthesis reconstruction; and 2) patients who underwent sub-periosteal tumour excision combining bone and soft-tissue ablation. Thigh STS in this study was defined as a lesion located below the plane of the lesser trochanter and above the plane of the femoral condyle. Well-differentiated liposarcoma and patients with metastatic disease at the time of presentation were excluded. For this analysis, STSs with only cortical contact of the adjacent bone based on preoperative imaging were included. All patients had at least two years of follow-up, except for those who reached the primary endpoint before two years post-surgery. A flowchart of inclusion and exclusion criteria is shown in Figure 1.

Imaging assessment

Determination of cortical contact was made based on MRI, which was evaluated and by consensus of two senior oncological specialists (YZM, LN). Image assessment for cortical contact was conducted as follows: cortical contact was defined as the the loss of normal tissue interface between tumour and the adjacent bone on T1-weighted MRI (Figure 2a). Cases with partial cortical thinning due to tumour involvement or compression, but without medullary invasion, were also included in this study. Cases where muscle or fat interposed between tumour and bone were excluded (Figure 2b). Cases with clear osseous invasion that extends into the medullary cavity, defined as increased signal intensity change presented on the normally hypointense cortical bone and medullary canal based on T1- or T2 -weighted images, were also excluded (Figure 2c). This approach ensured that patients with cortical contact without bone marrow invasion were included.

Variable measurement

Tumour grade was determined using the Fédération Nationale des Centres de Lutte Contre Le Cancer (FNCLCC) system.[9] Tumour size was measured according to the greatest dimension at the onset of treatment and evaluated with using the American Joint Committee on Cancer (AJCC) eighth edition criteria of bone and soft-tissue sarcomas (a: ≤ 5 cm, b: > 5 cm and ≤ 10 cm, c: > 10 cm and ≤ 15 cm, and d: > 15 cm).[10] However, only a small number of patients

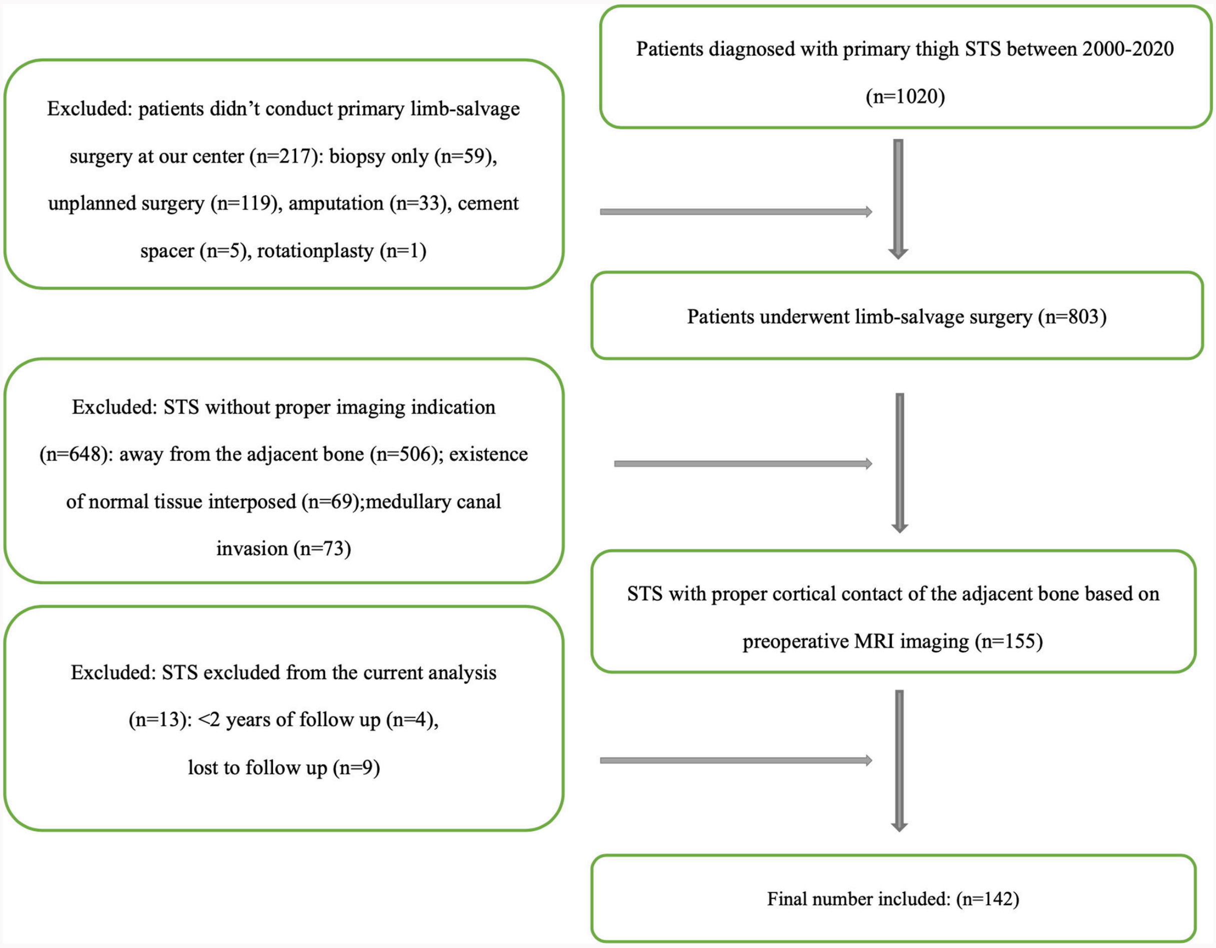

Fig. 1
Flowchart for patients included in this study. STS, soft-tissue sarcoma.

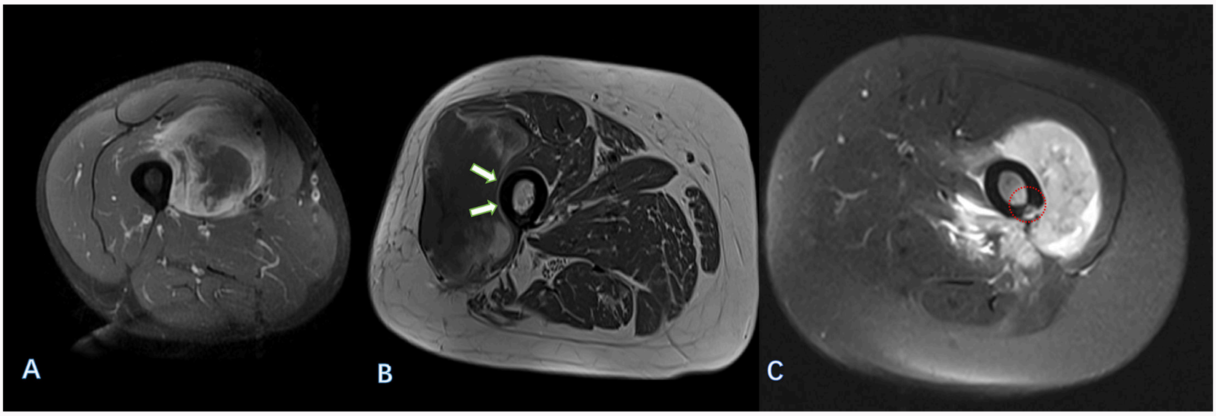

Fig. 2
Transverse section of MRI of soft-tissue sarcoma (STS) abutting the adjacent cortical bone. a) Tumour extending to the adjacent cortical bone without soft-tissue interface. This lesion had an approximately 33% circumferential abutment of the femur. b) A thin layer of normal soft-tissue (arrows) separates the tumour from the adjacent bone. No cortical contact was considered in this case. c) The circled area shows signal change in both the cortex and the medullary cavity, indicating STS with frank cortex destruction and medullary canal invasion.

had a tumour diameter ≤ 5 cm (n = 5) or > 15 cm (n = 12), therefore, 10 cm was selected as the cut-off value in multivariate analysis. To determine the extent of circumferential encasement of the femur, the tumour encasement angle was measured from 0° to 360°, and converted into a percentage ranging from 0% to 100%. (0% = no STS encasement; 100% = complete 360° encasement around the bone). For analysis purposes, circumferential cortical contact was categorized into two groups: ≤ 50% versus > 50%. Anatomical location-based factors were also included for prognosis analysis. The muscle involvement selected for analysis was based on the proximity to the femur and the clinical significance for surgical

Table I. Demographic details for all 142 patients stratified based on surgical approach.

Variable	No reconstruction (n = 105)	Reconstruction (n = 37)	p-value
Mean age, yrs (range)	54.0 (46.0 to 64.0)	53.0 (42.0 to 64.0)	0.287*
Sex, n (%)			0.641†
F	52 (49.5)	16 (43.2)	
M	53 (50.5)	21 (56.8)	
FNCLCC grade, n (%)			0.262†
III	55 (52.4)	24 (64.9)	
II	50 (47.6)	13 (35.1)	
I	0 (0.0)	0 (0.0)	
Size, n (%)			0.189‡
≤ 5 cm	3 (2.86)	1 (2.7)	
> 5 cm and ≤ 10 cm	16 (15.2)	3 (8.1)	
> 10 cm and ≤ 15 cm	81 (77.1)	26 (70.3)	
> 15 cm	5 (4.76%)	7 (18.9%)	
CCI, n (%)			0.290†
≤ 50%	87 (82.9)	27 (73.0)	
> 50%	18 (17.1)	10 (27)	
Full-course RTX, n (%)			0.095†
No	71 (67.6)	31 (83.8)	
Yes	34 (32.4)	6 (16.2)	
Full-course chemo, n (%)			0.183†
No	55 (52.4%)	14 (37.8%)	
Yes	50 (47.6%)	23 (62.2%)	
Histological diagnosis, n (%)			0.861‡
UPS	16 (15.2)	9 (24.3)	
Leiomyosarcoma	15 (14.3)	3 (8.10)	
Fibrosarcoma	15 (14.3)	3 (8.10)	
Rhabdomyosarcoma	10 (9.52)	2 (5.40)	
Pleomorphic liposarcoma	9 (8.57)	3 (8.10)	
Myxoid liposarcoma	8 (7.62)	3 (8.10)	
Myxofibrosarcoma	8 (7.62)	1 (2.70)	
Malignant fibrous histiocytoma	5 (4.76)	0 (0.0))	
Synovial sarcoma	4 (3.81)	0 (0.0)	
Ewing's sarcoma	0 (0.0)	4 (10.8)	
Chondrosarcoma	0 (0.0)	4 (10.8)	
Others	15 (14.3)	5 (13.5)	

*Independent-samples *t*-test.
†Chi-squared test.
‡Fisher's exact test.
CCI, circumferential cortical involvement; Chemo, chemotherapy; FNCLCC, Fédération Nationale des Centres de Lutte Contre Le Cancer; RTX, radiotherapy; UPS, undifferentiated pleomorphic sarcoma.

decision-making regarding bone resection. We, therefore, included muscles that directly connect to the femur from anterior, posterior, and medial compartments including the vastus lateralis, vastus intermedius, and vastus medialis, as well as those that attach to the periosteum of the femur via a common tendon including the adductor magnus, adductor longus, and adductor brevis. Lateral, posterior, and medial intermuscular septum were also included for analysis. No

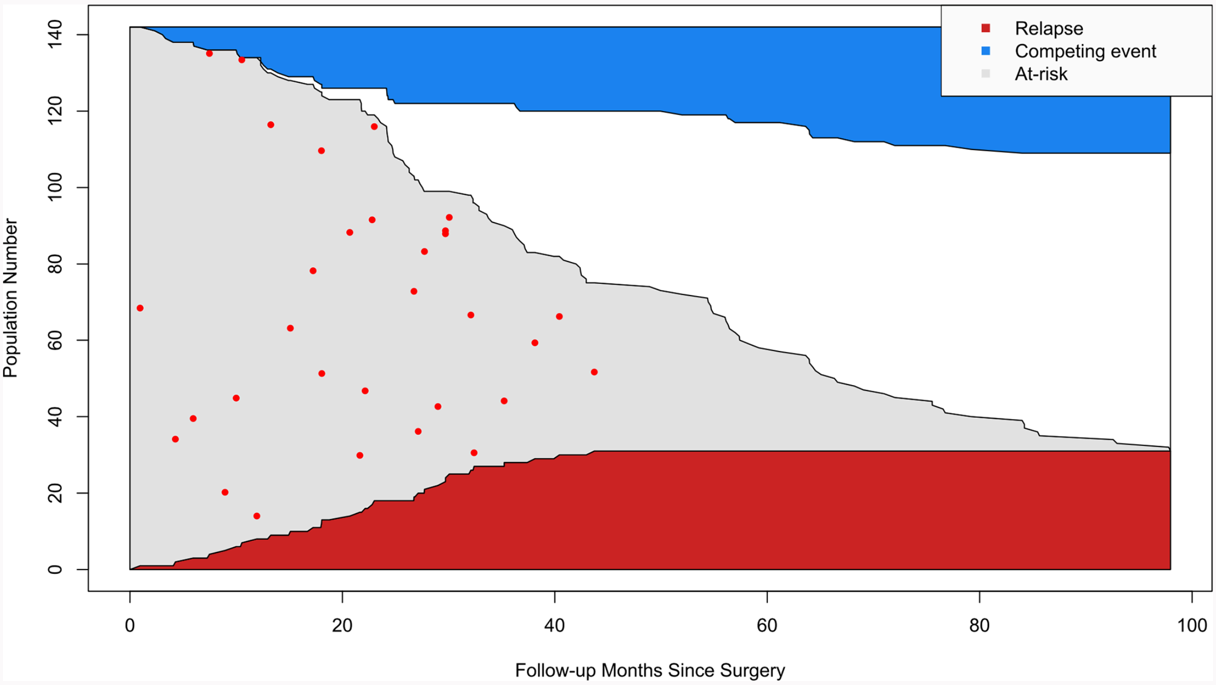

Fig. 3
Population-time plot showing the incidence density of relapse, with red dots indicating appearance of cases of recurrence throughout time. There were 36 cases of recurrence in our study.

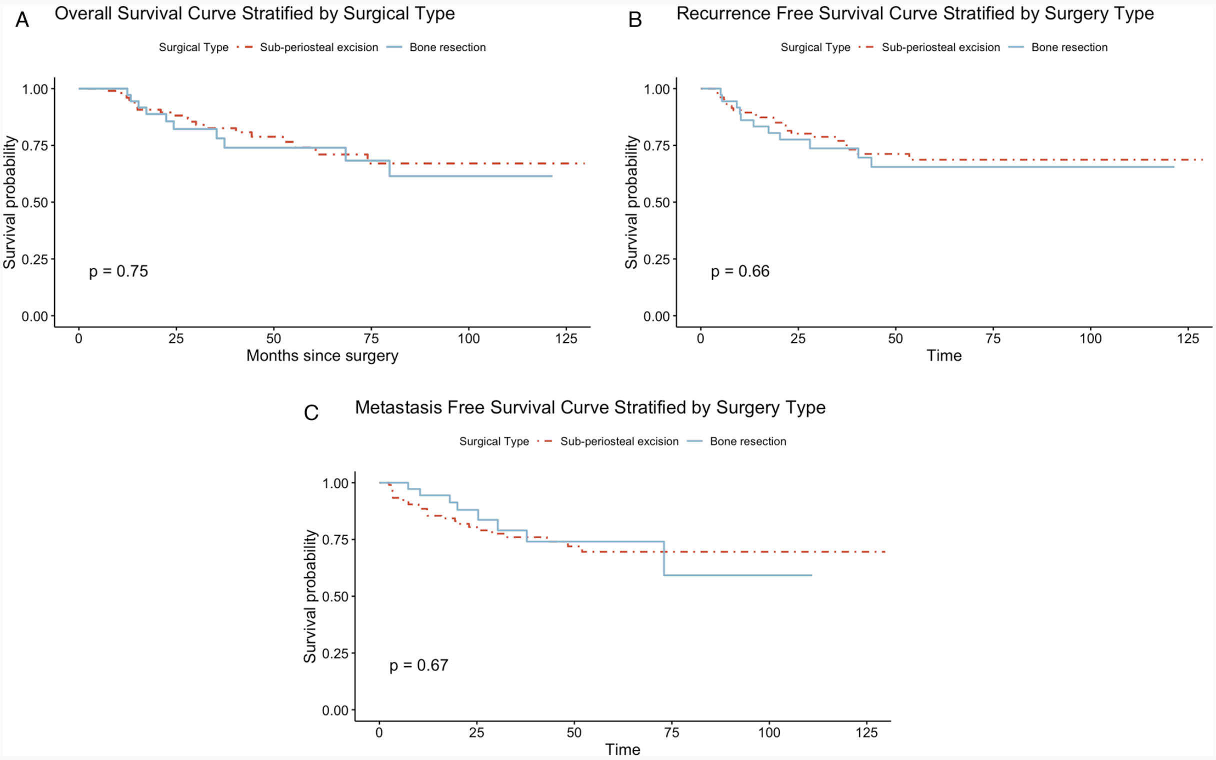

Fig. 4
Patients who underwent composite excision of soft-tissue sarcoma and the bone segment had similar a) overall survival, b) local-recurrence-free survival, and c) metastasis-free survival compared to those without bone resection.

preoperative radiotherapy was administered in this cohort considering poor adherence, delayed resection, and post-surgery wound complication. Postoperative radiotherapy was primarily recommended for patients who underwent sub-periosteal excision without achieving wide surgical margin. Chemotherapy was generally administered to STSs known to be sensitive to chemotherapy such as UPS, Ewing's sarcoma, leiomyosarcoma, and rhabdomyosarcoma. All the

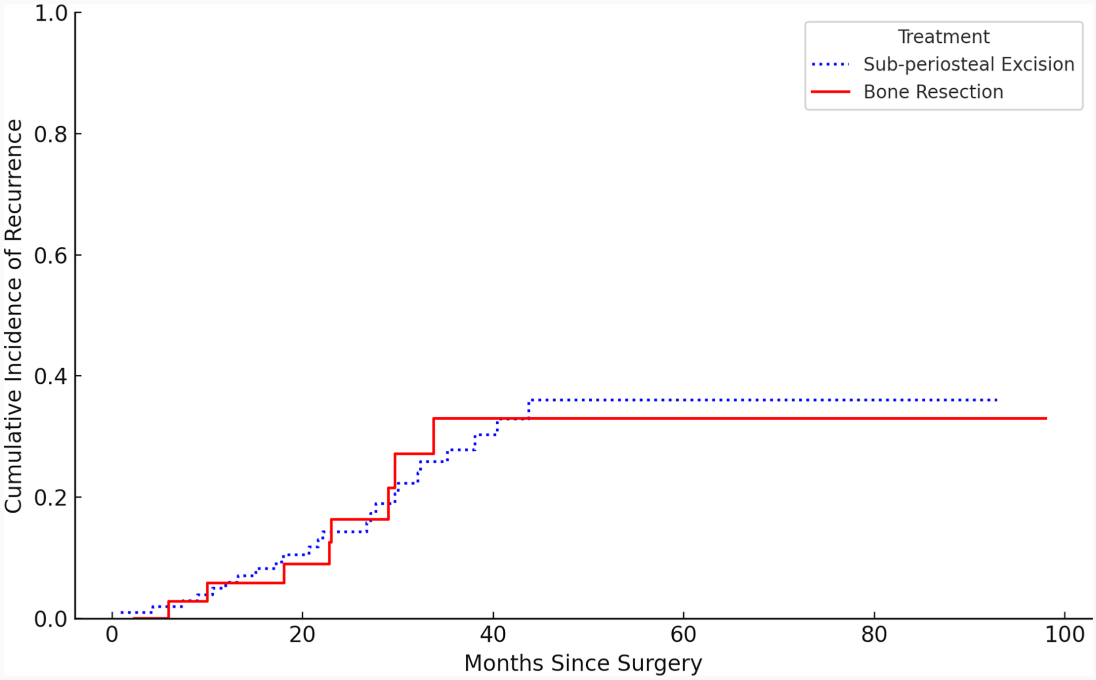

Fig. 5
Cumulative incidence plot for recurrence with death as a competing event between patients who underwent bone resection and those who did not.

adjuvant therapy plans were developed by consensus of a multidisciplinary team of specialists including medical oncologists, radiologists, and orthopaedic oncologists. The decision to resect bone or not took into account the extent of circumferential cortical contact and some important clinical factors, such as histological type, relationship with neighbouring major blood vessels and motor nerve, and tumour size, in combination with the likelihood of obtaining safe surgical margin without bone resection. Nevertheless, surgeons' decisions regarding bone sacrifice or preservation can vary significantly, even after taking all the above considerations into account. The Musculoskeletal Tumor Society (MSTS) score was used to assess patients' functional outcomes.[11]

Statistical analysis

Characteristic factors among patients who underwent bone resection were compared to those underwent sub-periosteal dissection. For continuous variables, either an independent-samples *t*-test or Mann-Whitney U test was conducted based on whether normal distribution was met. Categorical variables were analyzed using either chi-squared test or Fisher's exact test. Comparisons of overall survival, recurrence-free survival, and metastasis-free survival (MFS) were conducted using a log-rank test. Cumulative incidence of recurrence was conducted for two surgical approaches, using death as the competing event. Cox univariate and multivariate analyses were conducted to evaluate factors that were associated with overall survival, local recurrence, and metastasis. A Cox model, adjusting for tumour size, FNCLCC grade, and systematic therapy, was performed to determine the clinically independent prognostic factors for the aforementioned endpoints. MSTS scores were compared between groups using line plots. All statistical analyses were performed using R v.4.2.2 (R Foundation for Statistical Computing, Austria). Statistical significance was set at a p-value < 0.05.

Results

Clinical outcome

In the bone resection group, there were nine deaths (24.3%), nine recurrences (24.3%), and eight metastases (21.6%), compared to 22 deaths (20.9%), 27 recurrences (25.7%), and 25 metastases (23.8%) in the non-resection group. No significant differences in oncological outcomes were demonstrated between the two groups. The incidence density of recurrence is shown in a population-time plot (Figure 3). The effect of bone resection on overall survival, recurrence-free, and MFS is shown in Figure 4. The five-year overall survival (OS), local recurrence-free survival (LRFS), and MFS was 74.0%, 65.9%, and 74.1% for bone resection, respectively, compared with 72.9%, 68.3%, and 72.0% for sub-periosteal excision, respectively, with no statistical differences. The cumulative incidence of recurrence was 33.1% for bone resection and 36.4% for sub-periosteal excision at five years (Figure 5).

Prognostic factors for disease-specific survival, local control, and metastasis

In univariate analysis, FNCLCC grade was found to be associated with patients' survival, recurrence, and metastasis. For anatomical location-based factors, tumour growth into the medial intermuscular septum, vastus medialis, adductor longus, and adductor brevis was associated with local recurrence. Tumour invasion into the posterior intermuscular septum, vastus lateralis, and biceps femoris wasassociated with OS, and tumour growth into the posterior intermuscular septum and biceps femoris was associated with metastasis (Table II).

However, in the multivariate regression model with adjustment of histological grade, tumour size, and systematic therapy use, vastus medialis and adductor longus involvement lost significance with recurrence; intermuscular septum and biceps femoris involvement lost significance with survival; and

Table II. Univariate analysis of factors with the potential to affect mortality, recurrence, and metastasis.

Variable	Mortality					Recurrence					Metastasis				
	N	Event, n	HR	95% CI	p-value	N	Event, n	HR	95% CI	p-value	N	Event, n	HR	95% CI	p-value
Sex															
Female	68	18	N/A	N/A		68	20	N/A	N/A		68	18	N/A	N/A	
Male	74	13	0.555	0.272 to 1.134	0.106	74	16	0.655	0.339 to 1.265	0.207	74	15	0.704	0.354 to 1.397	0.315
Mean age (yrs)	142	31	1.014	0.989 to 1.040	0.279	142	36	1.019	0.968 to 1.013	0.118	142	33	0.978	0.955 to 1.002	0.078
FNCLCC															
II	63	6	N/A	N/A		63	9	N/A	N/A		63	8	N/A	N/A	
III	79	25	3.321	1.441 to 7.658	0.005	79	27	2.683	1.261 to 5.706	0.010	79	25	2.697	1.215 to 5.984	0.015
Radiotherapy															
No	102	27	N/A	N/A		102	31	N/A	N/A		102	28	N/A	N/A	
Yes	40	4	0.777	0.320 to 1.886	0.576	40	5	0.579	0.223 to 1.505	0.263	40	5	0.748	0.283 to 1.975	0.557
Chemotherapy															
No	75	22	N/A	N/A		75	21	N/A	N/A		75	19	N/A	N/A	
Yes	67	9	0.784	0.767 to 1.722	0.508	67	15	1.090	0.588 to 2.129	0.802	67	14	1.244	0.612 to 2.529	0.545
Reconstruction															
No	105	22	N/A	N/A		105	27	N/A	N/A		105	25	N/A	N/A	
Yes	37	9	1.103	0.541 to 2.541	0.687	37	9	1.070	0.597 to 2.777	0.685	37	8	0.842	0.380 to 1.867	0.672
CCI															
≤ 50%	114	24	N/A			114	31				114	27			
> 50%	28	7	1.121	0.48 to 2.61	0.791	28	5	0.562	0.218 to 1.45	0.232	28	6	0.822	0.34 to 1,99	0.664
Size															
≤ 10 cm	30	5	N/A	N/A		30	7	N/A	N/A		30	7	N/A	N/A	
> 10 cm	112	26	1.640	0.675 to 3.983	0.275	112	29	1.423	0.682 to 3.478	0.439	112	26	1.189	0.515 to 2.749	0.685
Medial septum															
No	96	20	N/A	N/A		96	14	N/A	N/A		96	18	N/A	N/A	
Yes	46	11	1.262	0.604 to 2.464	0.536	46	22	3.769	1.902 to 7.37	< 0.001	46	15	1.675	0.821 to 2.221	0.122
Posterior septum															
No	91	10	N/A	N/A		91	22	N/A	N/A		91	15	N/A	N/A	
Yes	51	21	3.826	1.800 to 8.134	< 0.001	51	14	1.784	0.620 to 2.319	0.625	51	18	2.448	1.229 to 4.875	0.011
Lateral septum															
No	115	26	N/A	N/A		115	28	N/A	N/A		115	26	N/A	N/A	
Yes	27	5	0.828	0.317 to 2.162	0.701	27	8	1.293	0.567 to 2.851	0.522	27	7	1.135	0.492 to 2.622	0.766
Vastus lateralis															
No	97	15	N/A	N/A		97	20	N/A	N/A		97	20	N/A	N/A	
Yes	45	16	2.965	1.473 to 5.798	0.003	45	16	1.677	0.895 to 3.347	0.123	45	13	1.313	0.652 to 2.646	0.446
Vastus intermedius															
No	54	10	N/A	N/A		54	11	N/A	N/A		54	10	N/A	N/A	
Yes	88	21	1.466	0.690 to 3.117	0.320	88	25	1.555	0.763 to 3.161	0.223	88	23	1.635	0.777 to 3.441	0.195
Vastus medialis															
No	76	14	N/A	N/A		76	13	N/A	N/A		76	14	N/A	N/A	
Yes	66	17	1.673	0.822 to 3.407	0.156	66	23	2.011	1.124 to 3.893	0.036	66	19	1.892	0.946 to 3.784	0.071
Adductor longus															
No	99	19	N/A	N/A		99	21	N/A	N/A		99	20	N/A	N/A	
Yes	43	12	1.163	0.563 to 2.405	0.683	43	15	1.993	1.024 to 3.881	0.042	43	13	1.725	0.804 to 3.483	0.129
Adductor brevis															
No	92	19	N/A	N/A		92	14	N/A	N/A		92	23	N/A	N/A	
Yes	50	12	1.190	0.577 to 3.011	0.649	50	22	3.351	1.708 to 6.536	0.002	50	10	0.800	0.380 to 1.681	0.555
Adductor magnus															
No	83	15	N/A	N/A		83	22	N/A	N/A		83	18	N/A	N/A	

(*Continued*)

(*Continued*)

Variable	Mortality					Recurrence					Metastasis				
	N	Event, n	HR	95% CI	p-value	N	Event, n	HR	95% CI	p-value	N	Event, n	HR	95% CI	p-value
Sex															
Yes	59	16	1.220	0.616 to 2.418	0.568	59	14	0.786	0.402 to 1.538	0.482	59	15	1.083	0.522 to 2.062	0.915
Biceps femoris															
No	102	16	N/A	N/A		102	26	N/A	N/A		102	16	N/A	N/A	
Yes	40	15	2.664	1.315 to 5.394	0.006	40	10	1.034	0.498 to 2.145	0.929	40	17	2.913	1.465 to 6.422	0.003

CCI, circumferential cortical involvement; FNCLCC, Fédération Nationale des Centres de Lutte Contre Le Cancer; HR, hazard ratio; N/A, not applicable.

biceps femoris involvement was no longer adversely associated with metastasis. As shown in Table III, OS was negatively associated with FNCLCC grade III (hazard ratio (HR) 2.784; 95% CI 1.128 to 6.870; p = 0.026) and STS growth through the posterior intermuscular septum (HR 2.804; 95% CI 1.293 to 6.077; p = 0.009). Recurrence was negatively associated with FNCLCC grade III STSs, STS growth through the medial intermuscular septum, and STS growth into the adductor brevis. As shown in Table IV, there was a 2.737-, 2.514-, and 2.248-fold risk, respectively, of increased recurrence for patients with FNCLCC grade III STSs (p = 0.009), STS growth through the medial intermuscular septum (p = 0.021), and STS growth into the adductor brevis (p = 0.042). Additionally, metastasis was negatively associated with FNCLCC grade III STSs and STS growth through the posterior intermuscular septum. As shown in Table V, there was a 2.364- and 2.129-fold risk of increased metastasis for patients with FNCLCC grade III STSs (p = 0.037) and STS growth through the posterior intermuscular septum (p = 0.034).

Functional outcomes

In terms of postoperative functional score, the mean MSTS score at final follow-up for patients who underwent bone resection was 24.7, significantly lower than the 28.3 for those without bone resection (p < 0.001). Also, patients who underwent bone excision had significantly lower scores in the subcategories of emotional acceptance, use of external support, walking ability, and gait alteration than those without bone resection (Figure 6).

Discussion

Osseous invasion has long been assessed as a prognostic factor in many studies.[6,7,12] It is well established that STS with bone invasion is associated with worse prognosis than STS without bone invasion.[7,8] Ferguson et al[7] reported in 2006 that histological bone invasion was associated with a poorer overall survival. However, definition of bone invasion across the literatures has been neither consistent nor clearly estalished. Specifically, these studies often fail to distinguish cortical involvement from medullary canal invasion. When it comes to STSs with bone invasion, in most studies, clear osseous invasion, particularly when involving the medullary canal, has been the primary focus, leading to a broad consensus for bone resection in such cases. In contrast, cases where the tumour extends only to the cortical portion have received limited attention.

In clinical practice, we frequently encounter cases where STS progresses towards the adjacent bone, pentrating the periosteum and compresing the cortex, yet without invading the medullary canal. This raises the question: does such cortical involvement truly constitute osseous invasion? Li et al[13] found that only medullary invasion, not cortical invasion, was associated with decreased overall survival in oral squamous cell carcinoma (OSCC). This leads us to theorize that, similar to OSCC, only medullary invasion may be associated with poorer prognosis in STS, which warrants more aggressive mangement. Unfortuantly, Li et al[13] failed to elaborate on their definition of 'cortical invasion', and it remains unclear whether their assessment was based on preoperative imaging or postoperative histology.

In our study, we use the term 'cortical contact' to reflect the limitations of preoperative imaging in determining true bone invasion. All STS cases included in this analysis were selected based on preoperative MRI findings showing close contact with the adjacent femur and loss of the normal tissue interface between the tumour and bone. However, preoperative MRI alone cannot reliably confirm whether actual invasion is present. In some cases, cortical thinning may be observed, which could be due to either tumour compression or true invasion, a distinction that can only be made through postoperative histological assessment.

This uncertainty complicates the decision to perform bone resection. During surgery, surgeons often observe tumour-induced irregularities on the periosteum and the surface of the cortex, while the deeper cortical layers and medullary canal remain intact. The extent of bone resection thus becomes a subject of debate. While some studies suggest that sub-periosteal resection with 'planned positive' margins provides local recurrence rates comparable to more extensive bone resection,[12] many surgeons still lean towards bone resection, particularly in cases of high-grade tumours, due to concerns about recurrence. However, they must also weigh the risks of postoperative complications and functional impairment from major skeletal defects and reconstruction.[14] As a result, determining the most appropriate surgical approach – whether to perform bone resection or adopt a more conservative method – remains a crucial decision for this subset of STS cases with cortical contact.

Our study excluded cases with definite evidence of medullary invasion and only included those with cortical contact on preoperative MRI, and found no significant difference in local recurrence, survival, or metastasis between two surgical approaches. Similar findings were reported by Lin

Table III. Multivariate analysis of factors with potential to affect mortality.

Variable	N	Event, n	HR	95% CI	p-value
FNCLCC					
II	63	6	N/A	N/A	
III	79	25	2.784	1.128 to 6.870	0.026
Posterior intermuscular septum					
No	91	10	N/A	N/A	
Yes	51	21	2.804	1.293 to 6.077	0.009

FNCLCC, Fédération Nationale des Centres de Lutte Contre Le Cancer; HR, hazard ratio; N/A, not applicable.

Table IV. Multivariate analysis of factors with potential to affect recurrence.

Variable	N	Event, n	HR	95% CI	p-value
FNCLCC					
II	63	9	N/A	N/A	
III	79	27	2.737	1.280 to 5.832	0.009
Medial intermuscular septum					
No	96	14	N/A	N/A	
Yes	46	22	2.514	1.152 to 5.488	0.021
Vastus medialis					
No	76	15	N/A	N/A	
Yes	66	21	2.292	0.898 to 4.905	0.083
Adductor brevis					
No	92	14	N/A	N/A	
Yes	50	22	2.248	1.031 to 4.905	0.042

FNCLCC, Fédération Nationale des Centres de Lutte Contre Le Cancer; HR, hazard ratio; N/A, not applicable.

Table V. Multivariate analysis of factors with potential to affect metastasis.

Variable	N	Event, n	HR	95% CI	p-value
FNCLCC					
II	63	8	N/A	N/A	
III	79	25	2.364	1.055 to 5.297	0.037
Posterior intermuscular septum					
No	91	15	N/A	N/A	
Yes	51	18	2.129	1.060 to 4.273	0.034

FNCLCC, Fédération Nationale des Centres de Lutte Contre Le Cancer; HR, hazard ratio; N/A, not applicable.

et al,[12] who reviewed 50 cases of STSs abutting adjacent bone. According to their results, there was no significant difference in local recurrence or survival between patients with and without bone resection, and only one recurrence resided in the vicinity of a previous bone contact region. However, cases with medullary canal invasion were included in Lin et al's[12] cohort, making the two surgery groups less comparable, as bone resection is clearly indicated in patients with medullary invasion. Of the 36 recurrences in this study, we found FNCLCC grade, extent of circumferential involvement, radiotherapy, and chemotherapy therapies were not significantly different between the two surgical groups. Nevertheless, we found that the proportion of patients with > 50% circumferential encasement tends to be higher among those with grade III tumours who underwent reconstruction, indicating a nuanced approach to surgical method based on tumour grade and circumferential involvement. We also carefully examined the imaging data and surgical profiles of the 36 recurrences and found no recurrence resided on the cortical bone, which suggests the lack of negative margin at the bone-tumour resection interface is not associated with risk of local recurrence. Additionally, among these patients, all presented with extracompartmental STSs, and 69.4% of STSs occupied the medial compartment and grew through either the posterior or medial intermuscular septum. Such increased ability to spread may be associated with recurrence.

Prognostic factors for STS outcomes have been well documented, but few studies have examined anatomical location-based factors.[13] Rimner et al[15] found that muscle compartment involvement did not influence mortality, recurrence, or metastasis in STS, whereas Morinaga et al[16] reported that STSs in the medial compartment were associated with worse MFS compared to those in the posterior or anterior compartments.[15,16] Our study differs by focusing specifically on tissue invasion relative to the femur in STS with cortical contact only. We found that tumour grade and invasion of the adductor brevis and medial intermuscular septum were risk factors for local recurrence, consistent with findings by Nakamura et al,[17] who identified a higher recurrence risk for STS in the adductor compartment. This increased recurrence risk might be explained by the proximity of tumours in the adductor region to major neurovascular structures like the sartorial canal or femoral triangle, making it difficult to achieve safe wide margins during surgery.[18] For vessel-sparing purposes, surgeons typically strip the tumour from the vessels, which compromises margin safety. Additionally, Alitalo et al[19] suggested interaction with the lymphatic vascular system may induce the spread of cancer cells to surrounding sites, which may explain such increased risk of recurrence in STSs arising within this region.

We also found that lesions invading the posterior intermuscular septum were associated with higher risk of mortality and metastasis. Patients with STSs that grew through the posterior intermuscular septum had worse survival and increased metastasis rate. No paper has reported similar results. We believe this poor prognosis might result from local failure. Among STSs that grow through the posterior intermuscular septum, only six (11.7%) were confined within one compartment. The remaining tumours all exhibited extension to neighbouring compartments, and some to major neurovascular bundle. Such extension beyond the confines of a single compartment could potentially contribute to higher

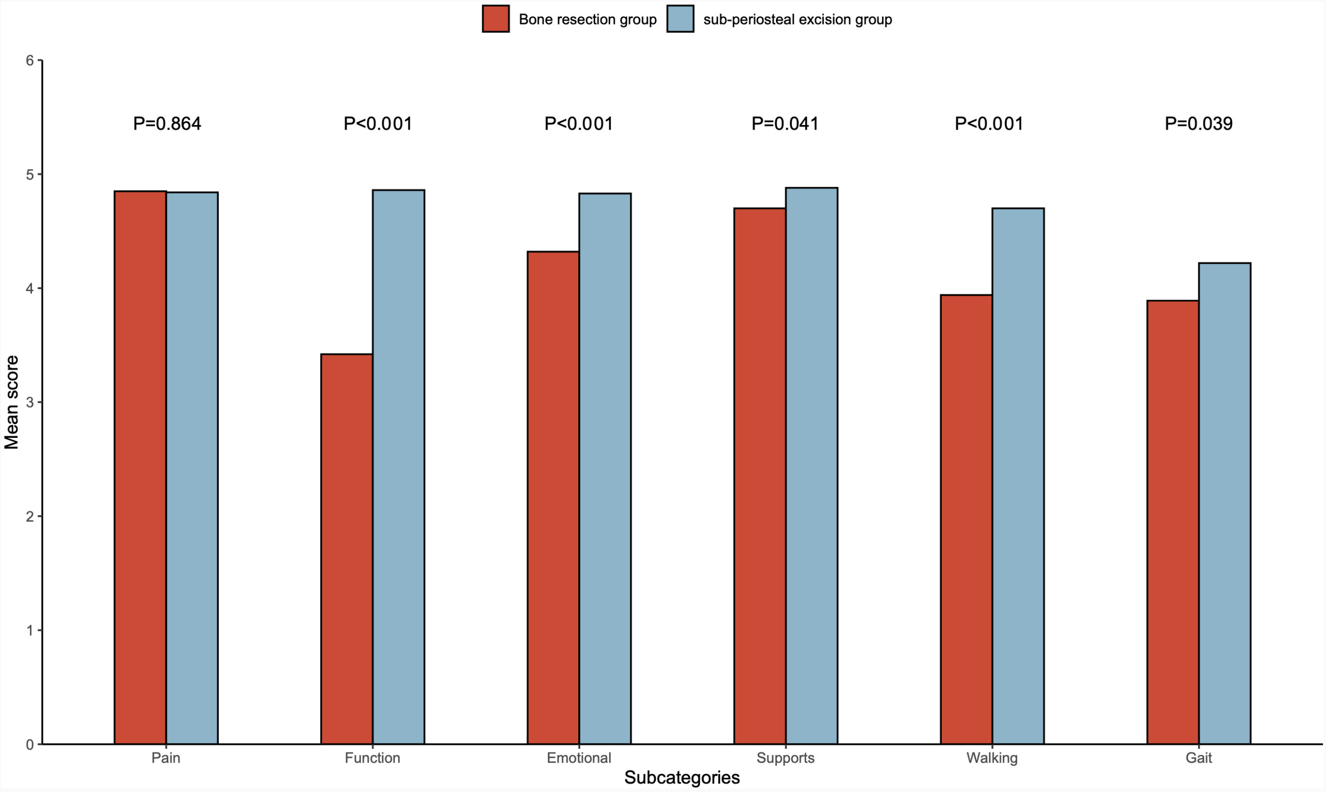

Fig. 6

The Musculoskeletal Tumor Society score results show significant differences between the bone resection group and the sub-periosteal excision group in function, emotional acceptance, walking ability, and gait, with p-values of < 0.001, < 0.001, 0.041, and 0.039, respectively. No significant difference was observed in pain scores (p = 0.864). Data are presented as mean scores for each subcategory.

risk of metastasis and mortality. Additionally, we found no difference in metastasis or mortality between patients with bone resection and those without. We believe that it is the expected less-than-wide margin around some major soft-tissue that potentially contributes to the incidence of metastasis and poorer overall survival, not the resection margin at the bone-tumour interface.

For thigh STSs with cortical contact, the primary goal for surgeons is to remove the tumour first and then restore limb function. Special attention should be focused on how to conduct complete tumour resection with minimal postoperative complications and functional impairment. In this cohort, 37 patients underwent composite bone resection and reconstruction surgery. Among them, seven received biological intercalary reconstruction, 12 received customized intercalary prothesis, and the remaining 28 underwent either proximal or distal femur endoprosthetic arthroplasty. While limb salvage surgery has advanced to an extreme stage of maturity, our findings indicate that, in comparison to those with sub-periosteal excision, patients undergoing bone resection exhibit significantly poorer outcomes in terms of function, emotional acceptance, use of external support, walking ability, and gait alteration, except for pain. Additionally, there were three cases of complications (two wound-related complications and one implant failure) observed in the bone resection group compared to zero cases in the non-resection group. We believe that patients who underwent bone resection failed to benefit significantly, and given the lack of definite improvement in prognosis, bone resection is not recommended in this specific type of STS.

Our study has several limitations. Given the complexity and rarity of STS, this cohort comprised patients with heterogenous diagnosis. Hence, we cannot ascertain whether some of the clinical outcomes observed are related to variations in STS histological types. Such biological diversity of STS and individual variations in patients, including economic considerations, inevitably lead to inconsistency in the systematic treatment regimens received by each patient, a challenge beyond the scope of retrospective study. Addressing this issue requires a large-scale prospective randomized controlled trial, yet such an endeavour would typically be hampered due to the rarity of STS, not to mention for the subset of STS with exclusively cortical contact.[20] Nevertheless, in our analysis, when comparing prognosis between two surgical approaches, no statistically significant difference was found between groups in terms of patients' demographics, which substantially helped mitigate potential bias. Furthermore, for various reasons such as cost concerns, poor adherence, or inconvenience, only 28% of patients completed the full course of radiotherapy, and 14% received partial radiotherapy, with 58% receiving no radiotherapy at all. Concerns regarding the lack of radiotherapy might influence the patient's prognosis. Fortunately, the proportion of radiotherapy between two surgical groups was similar, and hence, no statistically significant difference in prognosis can be attributed to disparity in radiotherapy use between the two groups; it is the impact of bone resection between two groups that matters the most.

In conclusion, for STSs in cortical contact with the femur, those with FNCLCC grade III, invasion into posterior intermuscular septum, medial intermuscular septum, and adductor brevis were found to be associated with poorer prognosis. Despite a potential concern of surgeons about the 'expected-positive' margin on the bone-tumour resection interface, all recurrent STSs emerged within the soft-tissue rather than on the cortical bone. Routine bone resection in this group of STSs does not lead to improved local control or survival, but does result in significantly compromised postoperative function. Therefore, an aggressive approach involving composite bone and tumour excision is not recommended in STSs with cortical contact of the adjacent femur on pre-surgery MRI, and sub-periosteal excision can result in a comparable local control and survival as bone excision approach.

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Data sharing

The datasets generated and analyzed in the current study are not publicly available due to data protection regulations. Access to data is limited to the researchers who have obtained permission for data processing. Further inquiries can be made to the corresponding author.

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Ethical review statement
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